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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,320	05/21/2001	Hidetoshi Uemura	UEMURA 4	6682

1444 7590 01/16/2003

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER
SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
1652	16

DATE MAILED: 01/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,320	UEMURA ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,20-22,25-53* is/are pending in the application.

4a) Of the above claim(s) *2,3,20-22,25-29,32-36,43-50,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,30,31,37-42 and 51* is/are rejected.

7)☒ Claim(s) *40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *0,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of Invention I, Claims 1, 30, 31, 37-42, and 51, as well as the protein species having the amino acid sequence composed of 229 residues represented by the 1st - 229th residues of SEQ ID NO: 2, in Paper No. 15 is acknowledged. The traversal is on the basis that Dillon, 1998 does not disclose a marker that is a serine protease but, rather, an arginase. This is acknowledged. However, the protein of Dillon is encompassed by the genus of proteins recited in Claim 1 as, no specific enzymatic activity is claimed for said genus of proteins. This issue is further described below under the U.S.C. 112 First and Second Paragraph rejections for Claim 1. The restriction requirement is still deemed proper and is therefore made FINAL.

Applicant's cancellation of Claims 3-19, 23, and 24 as well as amendment of Claims 20-22, 25, 30, 32-37, and 41 in Paper No. 7 is acknowledged. Applicant's addition of Claims 42-53 as well as amendment of Claims 20-22, 25, 30, and 32-35 in Paper No. 12 is acknowledged. Claims 2-3, 20-22, 25-29, 32-36, 43-50, 52, and 53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected Inventions, there being no allowable generic or linking claim. Claims 1, 30, 31, 37-42, and 51 are hereby examined.

Specification-Objections

Priority

Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country. Applicants have claimed priority to JAPAN 10/347802 filed November 20, 1998. Neither the Japanese application nor the translation of

JAPAN 10/347802, have been received. To obtain full benefit of the filing dates for JAPAN 10/347802 the original and translation of JAPAN 10/347802 should be submitted.

Title

The title is objected to for use of the word "novel" which, is redundant with a patent. Correction is required.

Abstract

The abstract is objected to for being a single run-on sentence. Correction is required.

Claims-Objections

Claim 40 is objected to for not ending in a period (.). Claim 40 is also objected to for the spelling "sperms"; the correct spelling is "sperm". Corrections are required.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which, the applicant regards as his invention.

Claims 1, 30, 31, and 37-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "same property" and "modified derivative" render Claim 1 indefinite as the property referred to and the modifications referred to are not defined. The term "several" in Claim 1 is an ambiguous term which, also renders the claim indefinite as, one of ordinary skill in the art, would not be reasonably apprised of the scope of the invention. In addition, the phrase "1st to 229th amino acids of SEQ ID NO: 2" is confusing, having more than one possible interpretation. It could mean residues 1-229 of SEQ ID NO: 2 or residues 54-282 of SEQ ID NO: 2. For these reasons, Claim 1 is rejected under 35 U.S.C. 112, second

paragraph. Since Claims 30, 31, and 37-41 are dependent on Claim 1, they are rejected for the same reasons. Examiner's note: for purposes of examination, it is assumed that Claim 1 recites residues 54-282 of SEQ ID NO: 2.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "peptide antibody" is confusing, having more than on possible interpretation. It could mean either a monoclonal antibody made recombinantly or a polyclonal or monoclonal antibody generated against a peptide fragment derived from one of the proteins recited in Claim 1. For purposes of examination, it is assumed that for Claim 31 the phrase "peptide antibody" refers to an antibody generated against a peptide fragment derived a protein recited in Claim 1.

Claims 42 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As described above for Claim 1, Claim 42 is rejected for reciting the phrase "1st to 229th amino acids of SEQ ID NO: 2". Since Claim 51 is dependent on Claim 42, it is rejected for the same reason.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 30, 31, 37-42, and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein set forth by residues 54-282 of SEQ ID

NO: 2, does not reasonably provide enablement for any protein derived from residues 54-282 of SEQ ID NO: 2 by addition, deletion, or substitution of amino acids, antibodies against said proteins, or pharmaceutical compositions comprising said proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 42, and 51 are so broad as to encompass any protein composed of residues 54-282 of SEQ ID NO: 2, any polypeptide having deletions, substitutions, or additions of said protein and having the same property of said protein or a modified derivative thereof or pharmaceutical compositions thereof. Claims 30 and 31 are so broad as to encompass any antibodies directed against said proteins or polypeptides. Claims 37-41 are so broad as to encompass any diagnostic marker comprising said proteins or polypeptides. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims,

and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the Claims 1 and 42 which, encompasses any polypeptide having deletions, substitutions, or additions of residues 54-282 of SEQ ID NO: 2, and having the same property of said protein or a modified derivative thereof. The specification does not support the broad scope of Claims 30 and 31 which, encompasses any antibodies directed against said proteins or polypeptides, the scope of Claims 37-41 which encompasses any diagnostic marker comprising said proteins or polypeptides, or the scope of Claim 51 which encompasses any pharmaceutical composition thereof.

The specification does not support the broad scope of Claims 1, 30, 31, 37-42, or 51 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the activity of bssp6; (B) the general tolerance of the activity of bssp6 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of proteins with an enormous number of amino acid

modifications of bssp6 as set forth by SEQ ID NO: 2, antibodies to said proteins, markers comprised of said proteins, and pharmaceutical compositions comprising said proteins. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1, 30, 31, 37-42, and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of protein molecules with the sequence set forth by residues 54-282 of SEQ ID NO:2 or any polypeptide having deletions, substitutions, or additions of said protein and having the same property of said protein or a modified derivative thereof and antibodies to any said proteins.

The specification does not contain any disclosure of the structure and function of all said proteins. The genus of proteins that comprise these above protein and polypeptide molecules is a large variable genus with the potentiality of having many different structures and activities. Therefore, many structurally and functionally unrelated proteins are encompassed within the scope of these claims, including partial polypeptide sequences. The specification discloses only a single species of the claimed genus which, is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one

skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1 and 37-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshida et al, 1998a. Yoshida et al, teach a serine protease protein having 100% identity with residues 54-282 of SEQ ID NO: 2. Therefore, Claims 1 and 37-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshida et al, 1998a.

Claims 1 and 37-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Davies et al, 1998a, Davis et al, 1998b, or Marra et al, 1996. Davies et al, 1998a and b teach a serine protease protein having 55% identity with residues 55-280 of SEQ ID NO: 2 while, Marra et al teach a serine protease protein having 91% identity with residues 116-270 of SEQ ID NO: 2.

Therefore, Claims 1 and 37-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Davies et al, 1998a, Davis et al, 1998b, or Marra et al, 1996.

Claims 1, 37-42 are rejected under 35 U.S.C. 102(a) as being anticipated by Bruck et al, 1999, Tang et al, 1999a, or Tang et al, 1999b. Bruck et al, Tang et al, a and b each teach serine protease proteins that have 100% identity with residues 54-282 of SEQ ID NO: 2. Therefore, Claims 1 and 37-42 are rejected under 35 U.S.C. 102(a) as being anticipated by Bruck et al, 1999, Tang et al, 1999a, or Tang et al, 1999b.

Claims 1 and 37-42 are rejected under 35 U.S.C. 102(a) as being anticipated by Hillman et al, 1999 or Brewer et al, 1998. Hillman et al teach a serine protease protein having 96% with residues 54-282 of SEQ ID NO: 2 while, Brewer et al teach a protein having 99% identity with residues 54-282 of SEQ ID NO: 2. Therefore, Claims 1 and 37-42 are rejected under 35 U.S.C. 102(a) as being anticipated by Hillman et al, 1999 or Brewer et al, 1998.

Claims 1 and 37-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al, 2000. Tang et al teach a serine protease protein that has 100% identity with residues 54-282 of SEQ ID NO: 2. The filing date for US Pat# 6075136 is October 6, 1997. Therefore, Claims 1 and 37-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al, 2000.

Claims 1 and 37-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Cohen et al, 2001 (US Pat# 6232456; Filing Date October 6, 1997), Darrow et al, 2002 (US Pat# 6420157; Filing Date August 31, 1999), Robison et al, 2001 (US Pat# 6331427; Filing Date March 26, 1999), or Southan et al, 2000 (US Pat# 6100059; Filing date April 8, 1998). Cohen et al teach a serine protease protein that has 97% identity with residues 54-282 of SEQ ID NO: 2. Darrow et al teach serine protease protein that has 97% identity with residues 54-282 of SEQ ID NO: 2.

Robison et al teach serine protease protein that has 73% identity with residues 77-278 of SEQ ID NO: 2. Southan et al teach serine protease protein that has 54% identity with residues 77-278 of SEQ ID NO: 2. Therefore, Claims 1 and 37-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Cohen et al, 2001, Darrow et al, 2002, Robison et al, 2001, and Southan et al, 2000 .

Applicants should note that Claims 38-41 have been included in all of the above rejections as the recitation of "to be used for diagnosis of..." are all intended use statements which fail to limit the scope of the claimed polypeptides in any way and, thus, have no patentable weight. The following rejections are further presented to address what appears to be applicant's interest in these claims, i.e. to recite proteins of Claim 1which, are expressed in particular cell types.

Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Davies et al, 1998b and 1998. The sequence taught by Davies et al, 1998a and 1998b is described above. Davies et al, 1998b also teach that their serine protease, BSP1, is expressed specifically in the hippocampus of the brain (Fig 2B). As stated by Davies et al, serine proteases are implicated in the patho-physiology of Alzheimer's disease in which early dysfunction of the hippocampus is a prominent feature (page 23004, paragraph 4). Since, BSP1 is expressed specifically in the hippocampus, degeneration of the hippocampus due to Alzheimer's disease would result in loss of BSP1. Thus, BSP1 is a marker for Alzheimer's disease. Therefore, Claims 37 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Davies et al, 1998b.

Claims 39-41 are rejected under 35 U.S.C. 102(a) as being anticipated by Tang et al, 1999b. The sequence taught by Tang et al, 1999a and 1999b is described above. Tang et al,

1999b also teach that their serine protease, PRASP, may be used for the diagnosis of disorders including abnormal spermatogenesis and abnormal sperm physiology as well as testicular cancer, prostate cancer, and cancers of the brain, heart, and testis (page 38, paragraph 4). Therefore, Claims 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al, 1999b.

Claims 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshida et al, 1998b. Yoshida et al, 1998b teach an antibody against a protein having the sequence set forth by SEQ ID NO: 2 with addition of amino acid residues encoding a hemagglutinin tag (Fig 4). Therefore, Claims 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshida et al, 1998b.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al, 1998b in view of Harlow, et al, 1988. The teachings of Yoshida et al are described above. Yoshida et al do not teach antibodies directed to all proteins composed of residues 54-282 of SEQ ID NO: 2 or all polypeptides having deletions, substitutions, or additions of said proteins. However, it is standard in the art to make antibodies to proteins (Harlow, et al 1988) and, thus, it would have been obvious to a person of ordinary skill in the art to use the method of Harlow et al to prepare an antibody to the protein of Yoshida et al. To do so is

suggested by Yoshida et al, 1998b, Fig 4, showing the use of antibodies directed to an hemagglutinin-tagged derivative of their protein for detection of tagged protein expression. Motivation to use the methods of Harlow et al to make antibodies against the protein of Yoshida et al derive from the ability to use said antibodies to detect the native, non-tagged protein; for example, in immunocytochemistry of tissue isolated from patients. The expectation of success is high because, preparation of antibodies is standard in the art (Harlow et al). Therefore, Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al, 1998b in view of Harlow, et al, 1988.

Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al, 1998b in view of Atkinson et al, 1998 and further in view of Suiden et al, 1992. The teachings of Yoshida et al are described above. Yoshida et al do not teach pharmaceutical compositions comprising their protein. However, it is standard in the art to make pharmaceutical compositions comprising enzymes (Atkinson, et al 1988) and, thus, it would have been obvious to a person of ordinary skill in the art to use the method of Atkinson et al to prepare a pharmaceutical composition comprising the protein of Yoshida et al. To do so is suggested by Yoshida et al and Suiden et al. Yoshida et al state that, their protein may be involved in neural plasticity (page 228, parag 2) while, Suiden et al teach that compositions comprising another serine protease, thrombin, causes neurite retraction in neuronal cells (Fig 1). Thus, a person of ordinary skill in the art would be motivated to test whether pharmaceutical compositions comprising the protein of Yoshida et al would affect neurite out-growth. The expectation of success is high as, preparation of pharmaceutical compositions comprising enzymes are common in the art (Atkinson et al). Therefore, Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being

unpatentable over Yoshida et al, 1998b in view of Atkinson et al, 1998 and further in view of Suiden et al, 1992.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1605